## II. THE OFFICE ACTION

In the Office Action, the Examiner maintained the restriction requirement, rejected claims 1, 15, 18-19, 24, 41-47 and 49-51 under obviousness–type double patenting and rejected claims 1, 15, 18-19, 24, 41-47 and 49-51 under 35 U.S.C. § 103 as obvious over Richter et al. (US Patent No. 5,705,518) in view of Levy et al. (U.S. Patent No. 5,283,255).

### A. Restriction/Election

The Examiner has maintained the restriction of the claims and has stated that the invention has been searched and examined to the extent that the invention is a method of treating onychomycosis as the disorder, skin as the tissue to be treated and fungus as the agent of exogenous origin and 5-aminolevulinic acid as the precursor of protoporphyrin IX. Without acquiescing to the position of the Examiner, non-elected claims 16, 17, 25, 26, 40 and 48 have been canceled without prejudice or disclaimer. Applicants of course reserve the right to file one or more divisional applications directed to the non-elected subject matter.

### B. Priority

The Examiner's acknowledgement of the claim for priority is appreciated.

### C. Double Patenting

The Examiner has rejected claims 1, 15, 18-19, 29-39, 41-47 and 49-51 under the doctrine of obviousness-type double patenting as allegedly claiming an invention obvious over U.S. Patent No. 5,955,490. It appears to be the position of the Examiner that the present claims and the claims of the parent comprise the same steps of treating the skin. Contrary to this assessment, the claims of US Patent No. 5,955,490 are directed to methods of treating acne, treating a disorder associated with Propino bacterium, treating malaria, treating a skin lesion associated with the presence of a bacterium, and treating a disorder associated with the presence of a parasite. In the present case, the elected method is directed to treating onychomycosis wherein the exogenous agent is fungus. Since the present election is directed to a method of treating onychomycosis (a fungal disorder) and the claims of U.S. Patent No. 5,955,490 do not teach or suggest treating onychomycosis, the obviousness-type double

patenting is improper here. Accordingly, reconsideration and withdrawal are respectfully requested.

**D. Rejections based on 35 U.S.C. § 103**

The Examiner has rejected claims 1, 15, 18-19, 24, 29-39, 41-47 and 49-51 under 35 U.S.C. § 103 as allegedly obvious over Richter et al. (U.S. Patent No. 5,705,518) in view of Levy et al. (U.S. Patent No. 5,283,255). Applicants respectfully traverse.

The Examiner asserts that Richter teaches using 5-aminolevulinic acid (5-ALA) to treat skin infections such as papilloma virus. Richter discloses that papilloma virus is effectively treated with a photosensitizer such as 5-ALA because the drug targets neovascular lesions. Fungi do not have vessels, and therefore, the teachings disclosed here would not be applicable to organisms without vascular systems. Even though the skin may contain a neovascular lesion which is treatable with 5-ALA, there is no reason for anyone skilled in the pertinent area to conclude that applying this method would in fact treat the fungus. Moreover, it is known in the literature that the vascular endothelium in animals does not readily produce protoporphyrin IX; therefore direct vascular effects and the targeting of neovascular lesions as disclosed here is unlikely to prove successful.

Levy does not remedy the lack of teaching of treatment of a non-vascular based lesion in Richter. Levy teaches the use of a group of hydromonobenzoporphyrins or "green porphyrins." These are externally formed, exogenous photosensitizers which are applied to the patient primarily by injection (because of their high molecular weight). With these compounds, the photoactive agent is administered directly and in final form, so achieving a photodynamic response is not dependent on the internal (either organ level or cellular level) synthesis of the actual active compound (as a metabolite). It depends merely on the delivery of the administered compound to the target site.

5-ALA, on the other hand, acts as a pro-drug. It is not active in and of itself. Administration of 5-ALA induces the formation at the cellular level within the body the formation of the actual active photosensitizer (protoporphyrin IX). Because the cellular mechanisms are quite different across the phylogenetic continuum (plants, animals, single cell

organisms, etc.), the behavior in the presence of 5-ALA is not the same throughout. Therefore, Levy, which teaches administration of an ***exogenous*** hydromonobenzoporphyrins, fails to teach or suggest administration of an ***endogenous*** precursor of protoporphyrin IX for the effective treatment of onychomycosis. Thus, would not have been obvious to one skilled in the art that application of 5-ALA to a fungus would be effective as described in Levy. Moreover, 5-ALA is a small, highly water soluble molecule. As compared to hydromonobenzoporphyrins, which are large, lipophillic molecules, 5-ALA may not even reach a potential target fungus as that described in Levy.

Therefore, because Richter teaches treating neovascular lesions with 5-ALA and Levy teaches treating fungal disorder with hydromonobenzoporphyrins, neither in combination or alone can Richter and Levy render the present invention obvious. Accordingly, reconsideration and withdrawal of the invention are respectfully requested.

## III. CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date June 13, 2002 By _____

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